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LETTER TO THE EDITORS

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Venous thrombosis as a complication of antiemetic treatment

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Although the frequency of acute emesis in highly emetogenic chemotherapy has decreased significantly since the application of serotonin (5-HT_3) antagonists and corticosteroids, delayed emesis remains a serious problem. Recently a multicenter study was initiated to test the efficacy of dexamethasone and granisetron for the prevention of delayed emesis.

The study was carried out in 120 patients. All patients were suffering from advanced cancer and were treated with cisplatin-containing chemotherapy. A group of 40 patients suffering from advanced ovarian cancer were treated with the so-called CP regimen (750 mg/m^2 cyclophosphamide and 75 mg/m^2 cisplatin given intravenously every 3 weeks). As an antiemetic regimen, 10 mg dexamethasone and 3 mg granisetron were given intravenously. After the first 24 h of each course, patients were treated orally with 1 mg granisetron in combination with 8 mg dexamethasone twice daily. According to the randomization procedure, placebo was given instead of granisetron during the first course only. Of the 40 patients, 3 (52, 47, and 49 years old, respectively) with advanced ovarian cancer appeared to have deep venous thrombosis of the leg at 2 or 3 days after the third or fifth course while the malignancy was responding well to chemotherapy. Only one patient used estrogens.

Thromboses and thromboembolic events in patients with a malignancy are well-recognized complications, and several explanations are possible. Endothelium and blood flow can be disrupted due to tumor compression or invasion, and activation of blood coagulation may occur with cancer. Certain conditions increase the risk of thrombosis in cancer patients, such as surgery, pancreatic cancer, and lung and mucin-producing gastrointestinal carcinoma [1]. As the malignancy was responding in all three of the aforementioned patients, these mechanisms seem unlikely.

Thrombotic complications can be precipitated by therapeutic interventions such as hormonal therapy or chemotherapy, especially combination chemotherapy. Recently, Coates and co-workers [2] described major thrombotic events in association with thrombocytopenia and renal failure following emetogenic chemotherapy and treatment with ondansetron, another 5-HT_3 antagonist. These authors rejected the possibility of a causative role for dexamethasone (which was prescribed) by citing two other studies in which dexamethasone (for only 1 day) was used and in which no thrombotic side effect was reported.

In older studies, thromboembolic complications have been reported in patients receiving cortisone or corticotrophin (ACTH) for nonmalignant diseases and in patients with Cushing's syndrome [3, 4]. Experiments with rats support a possible correlation with corticosteroids. High-dose dexamethasone treatment appeared to decrease fibrinolytic activity, resulting in increased blood-clot sizes in a venous thrombosis model and in an increased PAI-1 (plasminogen activator inhibitor type-1) level [5]. We therefore suggest a relationship between high-dose dexamethasone and the occurrence of thromboembolic complications.

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